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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,200	09/18/2003	Kerstin Kuhn-Wache	PBD-00027	7181

38724 7590 01/03/2006

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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 01/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,200	KUHN-WACHE ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-30 and 32-45* is/are pending in the application.

4a) Of the above claim(s) *32-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-30 and 41-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/18/05,11/24/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of species biguanides such as metformin, phenformin and buformin as an anti-diabetic agent, H-Ser-D-Glu-Thr-Gly-D-Val-D-Lys-D-Val-OH as a compound capable of binding to the secondary binding site of DPIV and diabetes mellitus as the metabolic disease with traverse, in the reply filed on October 31, 2005 is acknowledged. Examiner also acknowledges the cancellation of claim 31.

The elected species H-Ser-D-Glu-Thr-Gly-D-Val-D-Lys-D-Val-OH that binds to the secondary binding site of DPIV and DPIV like enzymes is free of art. Examiner extended the search to other species and found them to be free of art.

Claims 32-40 have been withdrawn from further consideration as being drawn to non-elected invention.

Applicants have argued that there is no serious burden to search inventions I and II together. Examiner believes that the subject matter of inventions I and II require search strategies that are different from each other. Search for each of the above inventions is not co-extensive particularly with regard to the non-patented literature search. Therefore, the restriction for examination purposes as indicated is proper and has been made final.

Sequence Compliance

Applicant is advised that the application is not in compliance with 37 CFR §§ 1.821-1.825.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR §§ 1.821- 1.825) in order to effect a complete response to this office action.

Specifically, SEQ ID Nos are missing from the amino acid sequences disclosed in the specification. Applicants are required to assign SEQ ID Nos to all amino acid sequences disclosed in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 26, 27, 29 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by US patent 6,376,549 issued to Fine, et al.

In the instant application, applicants claim a method for treatment of metabolic disease in a mammal comprising co-administration of a compound capable of binding to a secondary binding site of DPIV and DPIV like enzymes and at least one anti-diabetic agent.

Fine, et al., teaches a method and composition for the treatment diabetes that includes the anti-diabetic agent metformin and one or more of chromium, vanadium and magnesium (abstract). The reference also teaches compositions containing metformin along with vanadium and chromium exploit the insulin –like effects of vanadium and sodium. Metal ions such as vanadium, chromium and magnesium are capable of binding to the secondary binding site of DPIV and DPIV like enzymes. These ions can bind to negatively charged amino acid side chains of the secondary binding site, which is different from the active site, e.g. a) a receptor site or b) a substrate recognition site or c) a regulatory site or allosteric site, as disclosed in the specification. Therefore, the co-administration of metformin and one or more of chromium, vanadium and magnesium in a composition meets the limitations of the invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26, 27, 29, 30 and 41-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant application, applicants claim a method of treatment for metabolic diseases in a mammal by co-administration of a 'compound' capable of binding to the secondary binding site of DPIV and DPIV like enzymes and at least one anti-diabetic agent.

Applicants have claimed 'a compound' capable of binding to the secondary binding site of DPIV and DPIV like enzymes. Applicants have claimed 'a compound' in terms of function as being able to bind to the secondary binding site of DPIV and DPIV like enzymes with no structure given. The functions associated with the 'a compound' have been detailed in claims 41-45 with no structure of the compounds disclosed. Therefore, one skilled in the art would not be able to practice the invention as disclosed here, and convey to one skilled the art that the inventor(s) did not have the possession of the claimed invention at the time the application was filed.

Claims 26-30 and 41-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the present application, applicants claim a method of treatment for metabolic diseases in a mammal by co-administration of a compound capable of binding to a secondary binding site of DPIV and DPIV like enzymes and al least one anti-diabetic agent. Applicants have not disclosed how the DPIV secondary binding site compounds a-d are made, nor how any of these compounds could be used

in treating metabolic diseases. The disclosed experimental data (pages 80-98) does not correlate with the disclosed compounds of the invention. The specification provides no data on whether the combination therapy of the present invention is effective in treating the metabolic conditions.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (Wands, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a method of treatment for metabolic diseases by co-administering a combination of a DPIV secondary binding site compound and an anti-diabetic agent. The claims as recited encompass seven compounds as capable of binding to the secondary binding site of the DPIV and DPIV like enzymes. Of the seven compounds, three are peptides and 4 are compound represented by structures a-d. The specification does not disclose how the compounds represented by structures a-d are synthesized. The specification also does not support with evidence whether any of these compounds either alone or in combination with another anti-diabetic agent binds to the DPIV or DPIV like enzyme. Thus, the claims taken together with the specification imply that the applicants have not disclosed the invention to the full extent so that a person skilled in the art could practice the invention.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Arch, et al., (WO 01/97808 A1) teaches a method for the treatment of type II diabetes mellitus in mammal. Their method comprises of administering an effective amount of a dipeptidyl peptidase IV inhibitor and another anti-diabetic agent (abstract). Arch, et al., have disclosed several pyrrolidine and thiazolidide compounds as inhibitors of DPIV and biguanides as anti-diabetic agents for the combination therapy (page 12, claims 2-4). Such a combination has been shown to work in treating diabetes mellitus (pharmacological data presented on pages 10 and 11).

In the present application, applicants claim compounds that binds to the secondary binding site of the DPIV and DPIV like enzymes in combination with known anti-diabetic agents to treat metabolic diseases. The predictability of a combination of treatment is evident from Arch, et al. The unpredictability stems from the fact that the applicants have not disclosed how to synthesize compounds represented by structures a-d and have not furnished any experimental data to support the invention whether any of these compounds alone or in combination with the anti-diabetic agents work in treating the metabolic diseases as recited in the claims.

Since the uncertainty of the binding of the compounds to secondary site of the DPIV or DPIV like enzymes and the issue of the synthesis of compounds represented by structures a-d remains largely unsolved, means for treating the any or all of the metabolic disease conditions using the combination therapy is highly unpredictable.

(5) The amount of direction or guidance presented and (6) the presence or absence of working examples:

The specification has disclosed that the peptides are either synthesized or procured from the Bachem (Heidelberg, Germany). However, the specification does not provide details of how the compounds represented by the structural formula a-d are obtained for the intended use. The specification does not teach how to make other compounds that are capable of binding to secondary DPIV and DPIV like enzymes. In addition to this specification lacks disclosure of working examples to show how effective the combination therapy is, in treating the metabolic disease conditions recited in the claims.

(7) The quantity of experimentation necessary:

A combination of facts such as lack of disclosure of how to synthesize compounds recited in the claims and lack of experimental data to show that the compounds claimed in the invention either alone or in combination with anti-diabetic agent work in treating the disease condition introduces high unpredictability. Considering the state of the art as discussed by the applicants and the high unpredictability of the successful treatment of the metabolic diseases by using the combination therapy and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention.

It is the Examiner's position that one skilled in the art could not practice the invention commensurate in the scope of the claims without undue experimentation. It is also noted, considering the *a priori* unpredictability in the art with regard to making and using the compounds, that prevention and/or treatment of metabolic diseases using a compound that binds to the secondary site on the DPIV in combination with an anti-diabetic agent to treat metabolic disease conditions is not enabled.

Conclusion

Claims 26-30 and 41-45 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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